Phase I, Randomized, Parallel-group, Double-Blind, Placebo-Controlled, Single Dose Study to Evaluate the Blockade of CGRP Receptor by AMG 334 in Preventing PACAP-38 Induced Migraine-like Attacks in Migraine Patients

Published: 22-02-2016
Last updated: 17-04-2024

The primary objective of this study is to evaluate the inhibition of PACAP-38 induced migraine-like attacks by AMG 334Secondary objectives:* To evaluate the inhibition of PACAP-38 induced headaches by AMG 334* To evaluate the safety, tolerability,...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Headaches
Study type	Interventional

Summary

ID

NL-OMON45872

Source
ToetsingOnline

Brief title
20140207

Condition

- Headaches

Synonym
migraine

Research involving

Human

Sponsors and support

Primary sponsor: Amgen
Source(s) of monetary or material Support: Amgen

Intervention

Keyword: AMG 334, CGRP receptor, Migraine, PACAP-38 induced migraine like attacks

Outcome measures

Primary outcome

Occurrence of a migraine-like attack within 24 hours of challenge-agent

infusion

Secondary outcome

Secondary Endpoints:

* Occurrence of a headache within 24 hours of challenge-agent infusion

* Treatment-emergent adverse events

* Clinical significant changes in vital signs, ECGs, physical examinations,

laboratory safety tests and neurological assessments

* AMG 334 PK parameters, including C1 hour and AUC84d

* Anti-AMG 334 antibodies

Exploratory Endpoints:

* Severity of PACAP-38 induced migraine-like attacks and headaches

* Duration of PACAP-38 induced migraine-like attacks and headaches

* Migraine characteristics: localization, accompanying symptoms and

pre-monitory symptoms.

* PACAP-38 related treatment-emergent adverse events

* Evaluate the concentration of PACAP-38 and CGRP following administration of

AMG 334

Study description

Background summary

Migraine is a profound disabling disorder, episodic headache disorder with a one-year prevalence of 15-20%
in the Dutch population. Migraine is in the top 10 of the WHO most disabling diseases and belongs to the priority list
of under treated, serious disabling brain diseases. Migraine profylaxis is an area with a large "unmedcial need*.
Calcitonine Gene Related Peptide (CGRP) receptor antagonisme seems a good candidate to change that. The
investigated product AMG334 is an antagonist of the CGRP receptor by which it (besides other effects) could diminish
vasodilatation, pain transmission and inflammation in the brain and therefore could reduce migraine attacks.

See also the submitted document called "AMG 334_20140207_Rationale for Dose Selection and Amend 4"

Study objective

The primary objective of this study is to evaluate the inhibition of PACAP-38 induced migraine-like attacks by AMG 334

Secondary objectives:
* To evaluate the inhibition of PACAP-38 induced headaches by AMG 334
* To evaluate the safety, tolerability, pharmacokinetics, and immunogenicity of a single
intravenous (IV) dose of AMG 334 in migraine patients

Exploratory objectives:
* To evaluate the reduction in severity of PACAP-38 induced migraine-like attacks and headaches by AMG 334
* To evaluate the duration of PACAP-38 induced migraine-like attacks and headaches by AMG 334
* To evaluate the safety and tolerability of a single intravenous (IV) dose of exogenous PACAP-38

* To evaluate CGRP and PACAP-38 levels in migraine patients

Study design

This is a randomized, double-blind, placebo-controlled, parallel-group study in subjects with episodic migraines. This study will evaluate the efficacy of AMG 334 as measured by inhibition of PACAP-38 induced migraine-like attacks (MLA) after a single dose of AMG 334.

Part A: PACAP-38 Dose Selection Phase:
This phase was already completed in Belgium and the United States. The Netherlands will only particpate to part B

Part B:
* Phase 1: PACAP-38 challenge phase
The objective of this phase is to evaluate if subjects respond to PACAP-38 with a migrainelike attack within 24 hours after administration withe PACAP-38. For that purpose, subjects will be dosed on day 1 with 10 pmol/kg/min PACAP-38 during 10 minutes (total dose of 100 pmol/kg).
Subjects will leave the research center after the post-dose assessments on day 2 and will be asked to return on day 3 and day 8.
For subjects who did not respond to PACAP-38 with a migrainelike attack within 24 hours after dosing, the study will end on day 8 of this phase 1. For those who did respond, phase 2 will be started.

* Phase 2: Randomization (AMG 334 or Placebo) Phase:
A minimum of 16 and a maximum of 36 subjects will be randomized between two treatment groups (AMG 334 or placebo). On Day 1, treatment groups will receive 140 mg IV AMG 334 over 30 minutes or matching placebo, in a one to one allocation ratio. On Day 8, the subjects will be administered the dose of PACAP-38 determined from the PACAP-38 Dose Selection Phase. All subjects will remain in-house for 24 hours of observation following PACAP-38 infusion. Subjects will be monitored and at several timepoints asked questions from the headache questionnaire (Appendix D of the protocol), to determine if they have experienced a MLA. After 24 hours of data from the first 16 Randomized (AMG 334 or Placebo) Subjects challenged with PACAP-38 is available, an interim analysis will be conducted to determine if challenge rates are comparable to historical rates (~66%) and if AMG 334 has greater efficacy than placebo. If AMG 334 is found to completely block PACAP-38 induced migraines, or have the same efficacy as placebo, the study will be terminated. Otherwise, approximately 20 Randomized (AMG 334 or Placebo) Subjects will be added after confirmation that they are so called PACAP-38 responders at the end of phase 1.

Intervention

After informed consent has been obtained, all screening procedures and tests

establishing eligibility will be performed within a period of 21 days before study product administration.

Phase 1:
After predose procedures on Day 1, participants will receive a single dose of PACAP-38. PACAP-38 is administered as an intravenous (in the vein) infusion: 10 pmol/kg/min PACAP-38 over 10 minutes (total dose 100 pmol/kg).
Participants will be discharged upon completion of the study assessments of Day 2 and asked to return to the unit on Day 3 and on Day 8.
For those who do not responded to PACAP-38 with a migraine like attack within 24 hours after dosing, the study will end on day 8 of this phase 1. For those who did respond, phase 2 will be started.

Phase 2:
PACAP-38 responders from phase 1 will be randomized to receive either AMG 334 or matching placebo. Subjects will return to the research facility on Day -1, one day prior to investigational product administration, at which time baseline procedures will be
completed. After completion of all pre-dose procedures on the day of dosing (Day 1), subjects will receive AMG 334 or matching placebo. Subjects will reside at the research facility on Day 1 after dosing for at least 1 hour and then be discharged. Subjects will then return to the research
facility on Day 8 for the infusion of PACAP-38 and stay for at least 24 hours post PACAP-38 infusion and then discharged and provided with instructions to return to the research facility according to the procedures provided in the Schedule of Assessment (Table 4). Subjects will
be followed 85 days with three extra in-clinic (Day10, 29 and 57) study visits during that time. For a full list of study procedures, including the timing of each procedure, please refer to Protocol (dd. 21Oct2016) Section 7 and the Schedule of Assessments (Table 4).

Study burden and risks

See E9 in this ABR form and in section 4 of the Subject Information "Possible side effects and other undesirable effects/discomforts".

Contacts

Public
Amgen NV

Minervum 7061
Breda 4817 ZK
NL

Scientific
Amgen NV

Minervum 7061
Breda 4817 ZK
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* 18 to * 45 years of age at time of screening.
Migraine headaches without aura * 6 months prior to screening.
* 1 and * 5 migraine days per month in each of the 3 months prior to screening.

Exclusion criteria

History of migraine with aura, cluster headachte or hemiplegic migraine headache.
Other headache disorders (except for episodic tension-type headache <5days/month.
Recent nicotine or tobacco users (should have stopped approximately 6 months prior to screening).
Pregnant or breastfeeding women.
More exclusion criteria can be found on page 33 to 36 of the protocol amendment 4 dd 21Oct16

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-03-2017
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	AMG 334
Generic name:	not applicable

Ethics review

Approved WMO Date:	22-02-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-02-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-03-2017
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-10-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2014-004074-42-NL
ClinicalTrials.gov	NCT02542605
CCMO	NL56598.056.16